

### **REMARKS**

Claims 1-11 are currently pending in the application. Claims 5-11 have been withdrawn from consideration by the Examiner. Claims 3 and 4 are presently amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

The invention relates to the crystal structure of the 30S subunit.

#### ***Restriction Requirement***

The Office Action states that "It is assumed that Applicants inadvertently elected Group I, claims 1-11, and the inclusion of Claims 5-11 to Group I was a typographical error", and advises Applicants to revise the Response to Restriction Requirement to read Group I, claims 1-4. Accordingly, Applicants hereby state that in response to the Restriction Requirement dated January 21, 2003, Applicants elect Group I, Claims 1-4 for prosecution on the merits, with traverse.

#### ***Priority***

The Office Action acknowledges Applicants claim for foreign priority based on applications filed in the United Kingdom, and that said priority documents have been received by the Office. However, the Office Action notes that the following certified foreign priority documents, United Kingdom 0017376.5, filed 7/14/2000, and United Kingdom 0022943.5, filed 9/19/2000, are not in the applications, and that the priority can not be granted without certified copies.

Certified copies of foreign priority documents United Kingdom 0017376.5, filed 7/14/2000, and United Kingdom 0022943.5, filed 9/19/2000 are enclosed with this response. Accordingly, Applicants request that priority to these documents be granted for the instant application.

#### ***Objection to the Title***

The Office action asserts that the title of the invention is not descriptive because the title is directed to a crystal structure of the 30S ribosome and its use; however, the claims are directed to only the crystal structure of the 30S ribosome. As suggested by the Examiner, Applicants have amended the title to the following, "Crystal structure of the 30S ribosome". Removal of this objection is therefore requested.

***Claim Rejections-35 USC § 112, Second Paragraph***

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Office Action asserts that the recitation of the phrase "better(numerically less)" is indefinite because it is not clear what comparison the limitation "better" refers to. While not acquiescing to the rejection, and in order to more clearly define the claimed invention, Applicants have amended the claims to delete the word "better".

Claim 3 has been amended to recite "a crystal of 30S ribosomal subunit having a resolution numerically less than about 3 Å." Support for the structure of amended claim 3 is provided at p. 4, lines 10-14, wherein it is stated, "In a first aspect, the present invention provides a crystal of the *Thermus thermophilus* 30S subunit having a tetragonal space group P4<sub>1</sub>2<sub>1</sub>2 with unit cell dimensions of a = 401.375 Å, b = 401.375 Å, c=175.887 Å, or more generally about a =401.4 Å, b=401.4 Å, c=175.9 Å, but more preferably a =401.4 ± about 4.0 Å, b=401.4 ± about 4.0 Å, c=175.9 ± about 5.0 Å. An advantageous feature of the structure is that it diffracts beyond 3Å resolution."

In view of the above, reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejections-35 USC § 112, First Paragraph***

***Enablement***

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, enablement, because the office action asserts that "the specification, while being enabling for a crystal structure of the *Thermus thermophilus* 30S subunit having a resolution of 3.05 Å, which have the atom

coordinates instantly disclosed, does not reasonably provide enablement for any 30S subunit, or any 30S subunit having a resolution numerically less than about 3 Å”.

The Office Action further states that “claims 1, 2, and 4 contain the open claim language word “having” in line 1 of each claim, thus, including crystals, which contain more structure than the Table 1 defined structure”.

Applicants submit that claims 1-4 are properly enabled for a crystal structure of a 30S ribosomal subunit derived from *Thermus thermophilus*, as well as from other species. As of the earliest priority date of the instant application it was known that there was a high degree of conservation in the 30S structure (see Fujita et al., 1998; 9:3-12, Genome Inform. Ser. Workshop Genome Inform.; Altamra et al., 1991, J. Biol. Chem., 266:6195-6200; Moazed et al., 1987, Nature, 327:389-394; Lake et al., 1982, Proc. Natl. Acad. Sci. USA, 79:5948-5952; Woese et al., 1977, Proc. Natl. Acad. Sci. USA 74:5088-5090)..

The specification states at page 3, lines 7-9, [t]he 30S ribosomal subunit is a major target for antibiotics. The ribosome is a useful target for antibiotics since the **structure of the 30S is widely conserved between prokaryotes**, allowing for broad spectrum antibiotics. (emphasis added)”

The specification also states at page 9, lines 17,

“This methodology provides those of skill in the art a means to provide 30S crystals of *T.thermophilus*. **The conservation of ribosome structure, particularly regions of structure essential for function, between prokaryotes, for example prokaryotes which are human pathogens, such as *Staphylococcus spp*, and the like, allows the structure herein to be useful in the provision of anti-bacterial agents in general.** Thus, the structure may be used to solve 30S subunits by the technique of molecular replacement. In such a method, x-ray diffraction data are obtained from crystals of a 30S subunit from another species, e.g. a species of a bacteria pathogenic to humans. The coordinates of Table 1 may be used to find the orientation of the unknown

molecule in the crystal, and electron density maps calculated. These maps can then be interpreted with the sequence of the species in question, and the coordinates of the 30S structure described herein can be used to help and speed interpretation. In this way, the structure of the 30S subunit crystal of the invention facilitates the determination of structures of 30S subunits and whole ribosomes from other organisms. (emphasis added)”

In view of the high degree of conservation of ribosome structure known as of the filing date of the application, and disclosed in the instant application, one of skill in the art would accept that there is also conservation between the crystal structure of the 30S ribosomal subunit between prokaryotic species. In view of the above, Applicants submit that claims 1-4 are properly enabled for a crystal structure of a 30S ribosomal subunit derived from *Thermus thermophilus*, as well as from other species that have conservation in ribosomal structures.

In view of the above amendments, Applicants assert that claims 1-4 are properly enabled.

Claims 1-3 have been amended to replace the term “having” with the phrase “consisting of”.

The office action also asserts that “the specification is not enabled for those crystals beyond those which consist of a structure as defined by the coordinates of table 1”. Applicants note that a structure as defined by the coordinates of table 1 is recited in Claim 4, so Applicants contend that claim 4 is enabled. Further the instant specification discloses in the third paragraph of the summary section and in paragraph 60 the product with the limitations recited in amended claims 1 and 2, and discloses in the Materials and Methods Section how to make these crystals. Further, the instant specification also discloses how to use the structure information gained from the recited crystal products in the paragraphs located under the heading entitled “Functional Insight from the Structure of the 30S Ribosomal Subunit”.

### ***Written Description***

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, for lack of Written Description. The Office Action asserts that while Applicants disclose the crystal structure of the *thermus thermophilus* 30S subunit having a resolution of 3.05 Å, Applicants’ disclosure does not provide

written support for any 30S subunit having a resolution less than 3 Å. Applicants note that the third paragraph of the Summary Section discloses a crystal structure of the 30S ribosomal subunit having a teragonal space group as recited in claims 1 and 2, that diffracts beyond 3 Angstroms (recited above). Therefore, Applicants contend that Applicants' disclosure does indeed provide written support for a 30S subunit having a resolution less than 3 Å, and accordingly, requests reconsideration and withdrawal of the written description rejection.

***Claim Rejections-35 USC § 102***

Claim 3 is rejected under 35 U.S.C. 102(b), as being clearly anticipated by Clemons et al (1999).

Applicants submit that for a determination of anticipation to be proper, the prior art reference must disclose each and every limitation of the claim. *Atlas Powder Company et al. v. IRECO, Incorporated et al.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999).

The Office Action states that Clemons et al. teaches the crystal structure of a bacterial 30S ribosomal subunit at 5.5 Å is better than 3 Å. The Office Action asserts that Clemons et al. anticipates the limitation of "better" recited in Claim 3. However, Applicants note that claim 3 as amended, does not recite the term "better". Because claims 3 does not recite the term "better" and because Clemons et al do not teach a 30S ribosomal subunit having a resolution numerically less than about 3 Å, as recited in amended claim 3, Applicants contend that the Clemons et al reference does not anticipate newly amended Claim 3. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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